Remarks

Claims 1 and 4-11 were previously pending in the subject application. By this Amendment, the applicants have amended claim 11 and added new claims 12-14. Support for the amendments and new claims can be found throughout the subject specification and claims as originally filed. No new matter has been added by this Amendment. Accordingly, claims 1, 4-6 and 8-14 are currently before the Examiner. Favorable consideration of the claims now presented is respectfully requested.

The claim amendments set forth herein have been done in order to lend greater clarity to the claimed subject matter and to expedite prosecution. The amendment of the claims and the addition of new claims should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Initially, the applicants wish to note that the Office Action dated April 28, 2008 states that it is in response to the Amendment submitted to the Patent Office dated January 31, 2008. However, the Office Action does not specifically acknowledge that claim 11 was amended in that Supplemental Amendment dated January 31, 2008; therefore, the applicants are making the same amendments to claim 11 in this Amendment to make sure the amendment is entered into the record.

Claims 1, 5 and 11 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Mimoz *et al.* (*Anaesthesia*, 2001) and McLintock *et al.* (*British Journal of Surgery*, 1988) in view of Mather *et al.* (*Chirality*, 2000). The applicants respectfully traverse this ground for rejection because the cited references, either taken alone or in combination, do not disclose or suggest that nefopam has anti-emetic properties as claimed herein.

The Office Action relies on Mimoz *et al.* and McLintock *et al.* as teaching that nefopam is an anti-emetic agent. The applicants respectfully disagree with this interpretation of these references. In fact, those skilled in the art at the time of this invention knew that nausea and vomiting were well known side-effects associated with nefopam. See, for example, Pillans, P.I. *et al.* ("Adverse reactions associated with nefopam," The New Zealand Medical Journal, September 22, 1995, Vol. 108, No, 1008) (R6); Ghose, K. *et al.* ("An open pilot study of the preventive effect of nefopam in migraine headaches," Headache Quarterly, 1999, United States, Vol. 10, no. 3, pages 221-224,

ISSN:1059-7565) (R2); and Lasseter, K.C. *et al.* ("Nefopam HCI interaction study with eight other drugs," Journal of International Medical Research, 1976, Vol. 4, No. 3, pages 195-201) (R3). In fact, Mimoz *et al.* refer to the pro-emetic effect of nefopam.

Although it may be true that nefopam can be used in conjunction with morphine in a way that results in a reduction of side effects, the correct interpretation of the teachings of Mimoz *et al.* is that any reduction in nausea or vomiting is the consequence of a reduced dosage of morphine. It cannot be concluded from the cited references that nefopam is anti-emetic, and indeed that would be inconsistent with the teachings found in prior art references.

The cited references only suggest that the use of nefopam can reduce the amount of morphine needed — thereby reducing the side effects of morphine. Please note that any anti-emetic effect resulting from a reduction in morphine would have no relevance at all to claims 4, 12 and 13 wherein the patient is not receiving morphine. Furthermore, with regard to claim 14, the references teach nothing about treating dizziness and blurred vision.

There is no evidence in the prior art that racemic nefopam, much less (+)-nefopam, is anti-emetic. In fact, as noted above, nausea and vomiting are well-documented as deleterious side effects of racemic nefopam. Furthermore, because (+)-nefopam is generally considered to be more potent than (-)-nefopam (see, for example, Fasmer *et al., J. Pharm. Pharmacol.* 42(6):437-438, 1987; Rosland and Hole, *J. Pharm. Pharmacol.* 42(6):437-438, 1990; and Mather *et al., Chirality* 12(3):153-159, 2000) (copies enclosed), the only reasonable conclusion to be drawn from the prior art is that (+)-nefopam would be strongly pro-emetic. Therefore, it is very surprising that (+)-nefopam can be used according to the subject invention to actually treat nausea, dizziness, blurred vision and emesis.

It is well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.*

In view of the fact that the prior art, including the Mimoz *et al.* and the McLintock *et al.* references, did not teach that nefopam was an anti-emetic agent, there would be no reason for the skilled artisan to combine the teachings of Mimoz *et al.* and/or McLintock *et al.* with Mather *et al.* to arrive at the current invention.

It is also important to appreciate that the present invention does not involve the use of a single enantiomer, instead of the racemate, in a therapeutic application which is already known. To the contrary, the racemic was actually contraindicated for the use that is now claimed for the single enantiomer. The present invention is, in fact, contrary to every indication provided in the prior art. The discovery that (+)- is anti-emetic is genuinely surprising.

The cited references do not disclose or suggest the advantageous use of single enantiomer (+)-nefopam as now claimed by the current applicants. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on the Mimoz *et al.* reference and/or McLintock *et al.* in view of the teachings of Mather *et al.*.

Claims 4, 6 and 8-10 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Mimoz *et al.* (*Anaesthesia*, 2001) and McLintock *et al.* (*British Journal of Surgery*, 1988) in view of Mather *et al.* (*Chirality*, 2000) and further in view of Sridhar (*Cancer*, 1988). The applicants respectfully traverse this ground for rejection because the cited references, taken either alone or in combination, do not disclose or suggest the applicants' treatment method as claimed herein.

The shortcomings of the primary references, as those references related to the current invention, have been discussed above in detail. Specifically, these references provide no expectation that single enantiomer (+)-nefopam could be used to treat nausea, dizziness, blurred vision or emesis as claimed by the current applicants. In fact, this use is contrary to reports in the prior art that attribute these same unwanted side effects to the use of nefopam.

As noted above, the mere fact that the purported prior art could have been modified or applied in some manner to yield applicant's invention does not make the modification or application obvious unless the prior art suggested the desirability of the modification. *In re Gordon*, 221 USPQ 1125,1127 (Fed. Cir. 1984). An assertion of obviousness without the required suggestion or expectation of success in the prior art is tantamount to using applicant's disclosure to reconstruct the

prior art to arrive at the subject invention. Hindsight reconstruction of the prior art cannot support a §103 rejection, as was specifically recognized by the CCPA in *In re Sponnoble*, 56CCPA 823, 160 USPQ 237, 243 (1969).

As discussed in detail above, the Mimoz *et al.* and McLintock *et al.* references do not teach that nefopam is an anti-emetic agent. In fact, the prior art as a whole, suggested quite the opposite. Thus, the cited references do not suggest the desirability of the method claimed by the current applicants and provide no expectation of successful use of (+)-nefopam in treatment of nausea, dizziness, blurred vision and emesis. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on the Mimoz *et al.*, McLintock *et al.* and Mather *et al.* references in view of Sridhar *et al.*.

In view of the foregoing remarks, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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Attachment: Request for Continued Examination (RCE)